

**This Page Is Inserted by IFW Operations
and is not a part of the Official Record**

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

EXHIBIT B



88-819

MA

4:00 Removed from CSI for placement before coil
31 P MRS shows ~~little~~ injury - no injury

4:15 Normal T1W anatomy
- apparently MCA was not occluded. Therefore, finding
that SACS equally reduced signal intensity on T2W is
expected.

4:45 Transcatheter perforator with 40 ml 2% TTC
Brain removed & immersed in 2% TTC for 5 min after
20 min.
Initial impression is that MCA was not occluded.
No evidence of infarct in (R) cerebral hemisphere.
Brain stored in 10% buffered formalin.

~~XXXX~~ Preliminary histological analysis shows mild central ischemia/
necrotic damage. No injury to subcortical structures,
including basal ganglia, internal capsule. However,
evidence of subarachnoid hemorrhage, perivascular hemorrhage.

~~XXXX~~ Colour slides

2.3 kg m.

11:00

30 mg/kg Nimodipine i.v.
 arterial & i.v. femoral lines
 MCA surgery

1:28

MCA-O (R) with considerable bleeding; packed with gauze
 in CST
 MAP 90-95 mmHg

1:40

1/2 hour

1:58 start T₂W (2800/80)

2:03-2:06 4.6 ml 8043 (1 mmol/kg) i.v. MAP 90 → 79 → 85 mmHg
 CO₂ IMA-DAT T₂WI 2800/80 E24

OL 52 9-50 3/4
 inj D 5 min into sequence

2:15

B-DAT

" no apparent non-perfused areas. " immediate following A
 C-DAT " immediate following B

2:45 MAP 92 mmHg

CO₂ IMA D-DAT 253 " inj prior to start
 2:51- 4.6 ml 8043 (1 mmol/kg) i.v. MAP 102 → 87 → 92 mmHg
 2:54

E

immediately after D

3:10 MAP 97 mmHg

F

immediately after E

CO₂ IMA G-DATT₁ 600/20



68-713 m

3.2 kg M.

PERMANENT MCA-O : LACTATE MRT, 5043 mmHg

11:30 30 mg/kg Nembutal i.v.
 11:45 final internal & i.v. lines
 MCA surgery

12:58 MCA-O (R) thermocautery + cut.

3:25 in CSI & Hemo coil
 MAP \approx 100 mmHg

3:30 0.3 ml Nembutal i.v. MAP 100 \rightarrow 90 mmHg

3:40 MAP 106 mmHg

3:50 T2W coronal Multislice (TR/TE 2800/80, 100 x 100 FOV)
 MM67A shows cortical hyperintensity in MCA territory with
 ipsilateral LV closure

4:15 MAP 105 mmHg

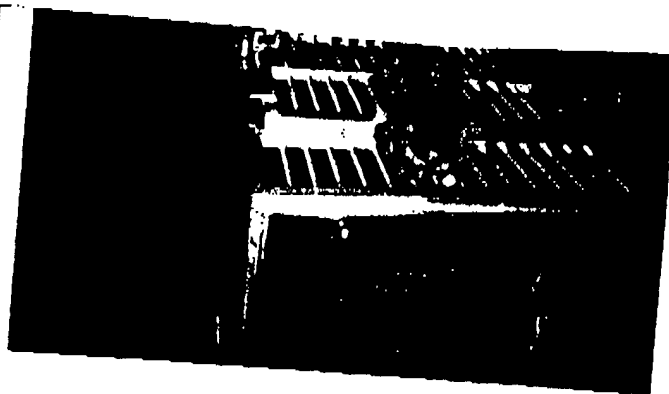
4:30 0.4 ml Nembutal MAP 107 \rightarrow 85 \rightarrow 101 mmHg

4:30 MAP 104 mmHg

5:15 MAP 113 mmHg

6:00 0.5 ml Nembutal MAP 115 \rightarrow 105 mmHg

\rightarrow Complete report from Mike Mosley's record



C0221*.dat

88-892 m

spectra
show lactate increase
+ rise in P.

$\frac{1}{2}$ Dose
A. dat
B. dat \Rightarrow pre-occ - pre - P_y
pre-occ ~~turning~~ + P_y C - H ✓

Need
pictures

TR/TE -
2000/100

3:03
3:20
3:40
4:00

C. dat - occ. + P_y

D
E
F

last pt. on washat curve

4:15 - start reperfusion
4:30 - intrus P_y
5:30
5:55

10 - N ✓
15 - O ✓
30 - P ✓
45 - Q ✓

C. dat
H. dat - no contrast
I. dat

change parameters
2000/100

HL = 50
OC = 50
CN = 50
NEX = 4
TC

spectra

2:00
2:30
3:40
4:00
4:55

.001 - pre-occlusion
.002 - pre
.003 - post-occ
.004 - post-occ
.005 -

H-1
P-31
P-31
H-1

OCCLUSION/REPERFUSION MCA PROTOCOL : S043

2.8 kg

11:05 30 mg/kg Nimodipine i.v.
 Temporal vein + artery catheters
 MCA surgery

Po
 ROI's

1:30 in CSI with suture line occluder snare positioned
 around @ MCA; suture externalised in polyethylene tubing
 MAP = 92 mmHg

CORR1A.DAT T₂W/I to check coil interaction.

2800/100 96 52 92 40
 3/4 0 offset pre-oc
 2:00 T₂W coronal multislabs shows partial @ LV closure + some more st.
 suggesting partial occlusion inadvertently.
 CORR1.DAT Lactate 2:00 pre-oc
 ↓ small lactate 40/80

2:20 P-31 MRS shows Pi at 4.7 ppm (slightly acidic); otherwise normal
¹H MRS shows very small lactate
 i.e. with MRI, spectroscopy suggests partial unobstructed
 occlusion

2:30 3P 2:30 pre-oc.
 1750 35

B.DAT T₂W/I 2800/80 any other in;

2:30-34 S043 (0.5 mmol/kg) = 2.8 ml MAP 95 → 86 → 94 mmHg.
 2:42 Start T₂W (2800/80)
 T₂W with S043 shows slight perfusion defect (high signal)
 in BG ipsilateral; LV partly closed; slight generalised inhibition
 mass effect
 3:03 occlusion & inj of O₂
 MCA-O @ +0.5 mmol/kg S043 over 4 min i.v. MAP 95 → 85 → 95
 C.DAT T₂W/I 2800/100 post w/o post oc

LO221D.DAT T₂WI immed after c
 LO221E.DAT T₂WI 2000/100 immed after D
 Start reformation / large increase in lactate
 4:00pm F.DAT T₂WI 2000/100
 4:30pm G.DAT T₂WI 2000/100 post reper post con
 4:55 .005 3p spectrum post reper
 .006 'H spectrum post reper
 5:24 H.DAT T₂WI 2000/100 post reper
 I.DAT T₂WI 2800/100 post reper
 .007 evaluate 'H spectrum 1DHS
 .008 " EC08
 .009 shorter TR

T2W collected from 3:04-3:16 (1-12 min post occlusion shows high signal (perfusion defect) at BG but not cortical structures)

T2W collected from 3:16-3:28 (13-28 min post occlusion shows little signal difference 13. plateau phase of SO4. Washout curve

- 3:40 P-31 MRS shows slight Pi elevation
4:00 2H MRS shows lactate elevation in + of Py
0.5mmol/kg SO43 i.v. over 3 min.
Start T2W (2000/100) coronal multisection
4:15 T2W (1-12 post SO43) shows progressive perfusion defect in cortical area level firstman; BG also hyperintense
4:15 attempted reperfusion by releasing snare around MCA.
MAP 102 mmHg
4:30 0.5mmol/kg SO43 i.v.
start T2W coronal multisection (2000/100)
1-12 min post contrast (reperfusion) shows T2W similar to post occlusion BG BG hyperintensity
5:05 P-31 MRS shows slightly elevated Pi at 4.7 ppm. - similar to pre-occlusion, thereby suggest improvement.
5:15 MAP 95 mmHg
5:30 T2W (2000/100) coronal multisection shows mild cortical hyperintensity - some mass effect, ipsilateral; BG still bright.
5:55 T2W (2800/100) same as 5:30
6:05 Removed from CAB
40 ml 20% TTE transcardially
Brom stained in 10% formalin
Dorsal infarction is cortical infarct

Note: proton spectra. lactate is evident, but overlapping fat is also present.



88-701 M

possibly a small amount of lactate

.003 'H post occ 1:22

.004 3IP post occ 1:28
B.DAT relatively normal spectra 2-50 9-40 2800/100

small decrease in PCr
rise in intensity in P_i region

3/4 1:40 post occ post con

More lactate

.005 reperfusion 'H 2:00

.006 reperfusion 3IP 2:07

Back to pre-occ. levels

Spectrum wrong

C.DAT 2:26

D.DAT

.007

.008

E

ROC1 9K 1500/80 NA2
H-1 323 EC08 1000/Tau 128 GN 500 60/120 50mm/3
Tau 192
E24 320 E24 2800/100 NA2 GN 40 0.52

lactate evident

.009

'H 4:15 after re-acc

.010

3IP 4:25

F.DAT

4:35

E24

2800/100

Evidence of injury again
decrease in PCr, rise in a peak at 3.007 ppm

2.6 kg M Occlusion/Reperfusion MCA : 5043

9:45 30 mg/kg Nembutal i.v.
arterial + venous lines
MCA surgery - upper respiratory congestion noted
(R) MCA loosely ligated & anastomosis; externalized in polyethylene tubing

12:00 cat placed in CS2
MAP 113 mmHg

CO227.001

1H spectrum pre-occlusion 12:40p-
Normal
31P pre-occlusion spectrum 12:50

CO227A.0AT

2C 50 2800/100 3/4
9040 1:05

1:15 MAP 115 mmHg

1:20 MCA - 0 (R) snare

1:35 MAP 116 mmHg

1H MRS shows no detectable lactate

31P MRS small increase in Pi at 4.77 ppm

1:40 1 mmol/kg dipyrizone DTPA i.v. (5.2 ml) MAP stable

1:42 MCA reperfusion

2:00 T2W coronal multislices shows signal hyperintensity lateral parietal cortex; otherwise, 5043 midline & lateral T2W signal loss outside MCA territory * soft tissue bilaminar
0.4 ml Nembutal i.v.
Poor gray-white differentiation

2:00 MCA reperfusion

2:10 normal proton MRS

2:20 31P MRS shows lowered Pi - apparently successful reperfusion

2:28 1 mmol 5043 (5.2 ml) i.v.

2:30 MAP stable at 115 mmHg

CO227-C 2:30 Start T2W (2800/100)

2:47 T2W shows minimal 5043-induced difference in high signal intensity compared to reperfusion state
still clear whether a perfusion successful
poor gray-white contrast

6-11-05

2000/100 image 5:20 no con

- 3:10 diffusion image suggests normal perfusion
 3:40 P-31 MRS suggests normal P_i / PCr .
 MAP 120 mmHg
 4:00 0.3 ml Nimblet i.v.
 4:10 T2W coronal multislides suggests minimal, if any, damage
 surface parietal cortex. (D)
 4:16 Re-occlusion MCA - Q (R)
 4:25 P-31 MRS shows elevated P_i
 4:40 1 mmol / kg SO43 i.v.
 4:20 T2W (2800/100) coronal multislides
 slightly higher signal intensity in cortical MCA territory
 Generally appears similar to 1st postocclusion SO43 T2W
 Poor grey/white contrast
 5:30 T2W (2000/100) shows only slight ipsilateral mass effect &
 cortical edema
 5:15 Removed from CSF
 perfused i.v. with blue dye
 Brain removed, shows absence of dye distal to MCA
 occlusion site. However, may also reflect some degree
 of hemorrhage induced by MCA transection just
 before sacrifice.
 Stained in 10% formalin overnight
 Colour slides



CØ 307.001

H-1 - pre-occlusion

Some lactate
present in
baseline
spectra

NA = 128
 $\tau = 128$

PWA90 = 40 msec.

CØ 307.002

PWA90 = 35 msec.

P-31 -

NA: 256

pre-occlusion
2 sec. rep. time

slightly elevated Pi in baseline

- pretty normal

CØ 307B.dat

1st image after occlusion
 $TR/TE = 2800/100$

CØ 307C.dat

OC - 50 GN-20
2nd multislice after occlusion
 $TR/TE = 2,000/100$

OC - 50
GN-20

CØ 307.003

CØ 307.004

H-1

P-31

CØ 307D.dat

$TR/TE = 2800/100$

OC - 50

GN-20

No. 2/slice

3/4

3:47
4:00

CØ 307.005

CØ 307.006

H-1

P-31

Occlusion/Reperfusion ACA- Kufenguta (CS2), N.K.
Sutcliffe, W. Chin.

CAT 88-849

- 1:00 Cat was hypoxic for 2-3 mins (He stopped breathing on the way down from Nakita's lab.)
- 1:05 Cat put on ventilator
- 1:20 Cat breathing on his own / placed in CSI
MAP - 110
- 1:30 CØ 307.001 H-1
1:40 CØ 307.002 P-31 Pre-occlusion / MAP 90
Pre-occlusion / MAP 90
- 2:00 CØ 307 A. dat T₂ TR/TE = 2800/80
- 2:10 MAP - 98 Pre-occlusion
- 2:24 120/98 MAP - 110 Note (Bespoke) 1H spectra indicator
- 2:25 Start ACA occlusion some lactate 312 - normal
- 2:28 start infusion D₂DTAA / started collecting of CØ 307 B. dat
MAP - 92
- 2:35 stopped infusion D₂DTAA
MAP - 92
- 2:41 CØ 307 C. dat TR/TE = 2,000/100
- 2:48 MAP - 94
- 3:00 CØ 307.003 H-1 → Lactate present
- 3:15 CØ 307.004 P-31 P_i slightly elevated
- 3:23 start reperfusion
- infusion of D₂DTAA (not a full dose! 2.5 ml's instead of 4 ml)
- 3:35 MAP - 105 - 89
- 3:37

~~XXXXXX~~ (cont.)

3:34 ~~5:48~~ CØ 307 D. dat - Post. ~~reper~~ reperfusion

3:48

4:00

CØ 307.005
CØ 307.006

H-1

P.31 reperfusion
P.1 decreased
slightly

4:35

CØ 307.007

4:45

CØ 307.008

H-1

P.31

looks like full recovery

5:30

CØ 307.009

5:40

CØ 307.010

H-1

P.31

6:00

CØ 307 E. dat

final

image

(Backup on SH/SH
disk)

TR/TE = 2800/100

Histology: MCA snare was inadvertently pulled while moving the animal from magnet. MCA was apparently transected. Subsequent TTC perfusion showed massive hemispheric infarct probably unrelated to actual experimental lesion. Brain stored in formalin.

~~XXXXXX~~ Colour slides indicate total hemispheric infarct in MCA territory.

~~Do~~
1:01 Cat pt in magnet

1:35 'H- 00316.001

Rs8747e

Do this only
Third slice

Image #3

	1	2	3	4
5950.50				
3370.37				
4497.75				
4735.12				
4705.25				
A	5839.37	4558.00	6430.12	6087.5
B	3397.00	3453.37	3786.50	3651.3
C	4309.25	3585.62	4784.50	4526.15
D	4572.12	3687.62	5023.25	4586.6
E	4531.00	3649.62	5139.62	4614.5
A'	5893.75	4681.00	6210.37	5935.0
B'	3341.50	3316.25	3337.00	4260.6
C'	4305.37	3768.50	4830.37	4873.1
D'	4629.12	3704.62	4930.5	4889.7
E'	4908.62	3927.12	4801.25	5014.2

Image #4

	1	2	3	4
A	5305.37	4752.37	6048.37	5841.75
B	3457.12	3831.37	3601.12	3355.75
C	4233.62	3970.50	4622.12	4555.25
D	4179.37	3822.25	4485.75	4239.00
E	4537.37	3840.12	4588.37	4575.5
A'	5689.62	4819.62	5925.37	5352.0
B'	3870.62	3300.12	4030.75	3872.62
C'	4480.50	3827.12	4971.37	4198.00
D'	4530.50	3972.62	5273.12	4733.50
E'	4532.50	4188.12	5446.50	4720.62

Image #1	MAG2	1	2	3	4
		3784.12	3510.12	5100.5	4591.75
	N	2977.37	2845.5	3058.5	3417.87
	O	3062.75	3456.37	4900.5	4189.62
	P	3811.37	3357.12	4794.6	4432.87
	Q	3070.50	3228.62	5017.12	4305.75
	R	1	2	3	4
	N	3729.25	3023.25	5084.75	5352.12
	O	2899.25	2774.62	3252.87	4703.25
	P	3069.75	3448.87	4586.25	5303.12
	Q	3733.75	3447.5	4993.5	5395.62
	R	3054.25	3381.62	4874.75	4800.57

Image #2	MAG2	1	2	3	4
		3582.75	2302.65	4009.62	4292.00
	N	2817.12	2757.87	2977.12	3055.12
	O	3386.25	2973.5	4351.00	4005.62
	P	3037.00	2921.62	4015.5	3982.62
	Q	3768.12	2928.37	4207.00	3965.37
	R	1	2	3	4
	N	3345.62	3050.75	4545.25	4314.75
	O	2689.87	2790.0	4002.75	4779.75
	P	3320.75	2961.87	4539.5	4400.75
	Q	3445.12	2982.75	4651.62	4600.12
	R	3273.37	2781.12	4358.5	4336.12

Image #3	MAG2	1	2	3	4
		4518.12	3020.25	5221.25	4641.12
	N	2941.62	3115.37	3187.87	3167.12
	O	4052.75	3522.37	4686.75	4228.37
	P	4179.25	3010.37	5015.75	4477.8
	Q	4003.75	3373.25	4797.5	3990.6
	R	1	2	3	4
	N	4959.62	4423.50	5301.87	5121.75
	O	3432.87	3599.00	3110.62	5335.12
	P	4370.62	4153.00	4307.75	5547.37
	Q	4642.12	4204.87	4568.12	5301.75
	R	4590.00	4231.50	4883.25	5153.25

Image #1

MAG2

N
C
C
R
N
C
C
R

1	2	3	4
4298.25	3727.62	482.87	4530.25
3146.25	3187.25	3217.62	3299.75
3925.75	3689.12	4019.00	4186.75
4222.12	3960.37	4272.12	4370.00
4012.37	3730.0	4304.12	4291.87
4506.62	4320.12	5071.5	4990.00
3528.6	3181.37	2850.12	4781.75
4327.25	4095.12	4389.37	5025.00
4370.00	4297.37	4757.62	4820.62
4096.5	4120.37	4607.75	4454.75

MAG2 ROI Redone

1 NRG

2 N White

3 N Sulcus

4 N Grey

Slice #3

✓ F
✓ U
✓ V
✓ W
✓ X

✓ A
✓ B
✓ C
✓ D
✓ E
✓ N
✓ P
✓ Q
✓ R

1' INS RS

2'

3'

4'

NBG			N White			N Sulcus		
Time	0	N	4483.0					
Chn.	15	O	2940.87		3550.37		5533.37	450
	30	P	4023.75		3100.37		3908.37	3011
	45	Q	4139.87		3403.12		4880.02	402
	75	R	3994.6		3001.12		5124.37	42
					3294.87		4822.37	42
INS BG			INS White			INS Sulcus		
		N	4915.3	500.12	3914.87		5533.37	512
		O	4503.37	4750.87	241.57		5388.02	553
		P	4756	4607.5	3514.87		5524.75	550
		Q	5089.75		3792.12		5514.12	532
		R	4859.12		3813.12		5192.02	51
			4870.00		3805.75			
NBG			N White			N Sulcus		
		A	4500.00		4574.5		4917.12	4526
	15	B	4300.87		3579.5		35295.35	4583
	30	C	4507.95		3605.8		5349.02	4614
	45	D	4513.25		3682.25		5562.75	4785
	75	E	4507.75		3614.00			
INS BG			INS White			INS Sulcus		
		A	5010.37	500.00	31092.37		5335.37	4941
		B	4595.25		3815.02		5440.12	489
		C	4825.25		3905.58		5537.02	494
		D	4924.87		3783.37		5005.02	500
		E	5111.02		4030.87			

half			dose immediately after occlusion		
NBG			N White		
	0	B	3100.12		
	15	C	1892.87		
	30	D	2480.12		
	45	E	2727.37		
	60	F	2185.02		
INS BG			INS White		
	0	B	3539.02		
	15	C	2721.87		
	30	D	2974.75		
	45	E	3201.75		
	60	F			
N Sulcus			N Sulcus		
			2208.75		2415.02
			2031.75		1681.75
			2439.02		2275.75
			2531.25		2408.37
			2300.5		2400.5
INS Sulcus			INS Sulcus		
			2229.37		2421.37
			1914.75		1593.02
			2240.37		2102.02
			2344.25		2583.5

ROI's $\frac{1}{2}$ dose R₂/BC only
slice 4 C0221*. dat

C C0221 ~~B~~ -
 15 N4C -
 30 04D -
 45m. Q4E -

NBC
 3324.57
~~1805~~ 1522
 1865
 1951

IBC
~~2504.12~~ 3049.25
 2378
 2465
 2398.